REMARKS

Claims 31, 34-35, 38-39 and 51-52 and 57-59 were pending in the application. Claim 59 has been canceled without prejudice, claims 38, 57 and 58 have been amended, and new claim 60 has been added. Accordingly, upon entry of the amendments presented herein, claims 31, 34-35, 38-39, 51-52, 57-58 and 60 will remain pending in the application. As indicated by the Examiner at page 1 of the present Office Action (dated January 30, 2008), claims 34 and 35 are allowable.

Claim 38 has been amended to depend from claims 31, 34, 35 and 60.

Claims 57 and 58 have been amended to specify that the antibody encompassed by the molecular conjugate is a *human* monoclonal antibody that comprises *heavy and light chain variable regions*. Support for the amendments to claims 57 and 58 can be found throughout the application as filed, for example, in Figure 13.

New claim 60 is drawn to a molecular conjugate comprising a monoclonal antibody that binds to the human macrophage mannose receptor, *linked to NY-ESO-1 antigen*, wherein the antibody comprises particular heavy chain and light chain variable region sequences. Support for new claim 60 can be found throughout the specification and claims and originally filed, for example, at page 39 (lines 1-5).

No new matter has been added. The foregoing claim cancellations should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the application. Applicants reserve the right to pursue claims to the canceled subject matter, or any subject matter which they are entitled to claim, in this or a separate application.

Acknowledgment of the Examiner's Withdrawal of Certain Rejections and Objections

Applicants gratefully acknowledge the Examiner's withdrawal of the following rejections: (a) the previous rejection of claims 27-30, 32, 33, 38, 39, 51 and 52 as being unpatentable over U.S. Patent No. 5,922,845 in view of Tuting *et al.* (1998) and Sallusto *et al.* (1995); (b) the previous rejection of claims 27-30, 32, 33, 38, 39, 51 and 52 as being unpatentable over U.S. Patent Application Publication No. 2002/0187131 in view of U.S.

Patent No. 5,922,845 and Tuting *et al.* (1998); and (c) the previous rejection of claim 32 under 35 U.S.C. § 112, first paragraph, as containing new matter.

Allowable Claims

Applicants acknowledge with appreciation the Examiner's indication that claims 34 and 35 are allowable.

Withdrawal of Previous Allowance of Claim 31

At page 2 of the present Office Action, the Examiner has indicated that the allowance of claim 31 has been withdrawn based on obviousness-type double patenting issues over Applicants' copending claims in Application No. 10/903,191.

However, as discussed below in the section addressing this provisional obviousness-type double patenting rejection, Applicants respectfully submit that when the remaining pending claims in the present application are indicated allowable, Applicants will submit, if appropriate, a terminal disclaimer over U.S. Patent Application No.: 10/903,191.

Objection to the Specification

The Examiner asserts that the specification fails to provide proper antecedent basis because, according to the Examiner, "[t]he molecular conjugate of claim 31 is not disclosed in the specification."

Applicants respectfully traverse this rejection. Contrary to the Examiner's assertion, claim 31 (drawn to a molecular conjugate comprising a human monoclonal antibody that binds to human dendritic cells, linked to an antigen, wherein the antibody is defined by particular heavy and light chain variable regions sequence (*i.e.*, SEQ ID NOs:2 and 4) is fully supported by the specification and claims as originally filed. Specifically, explicit support for claim 31 can be found, for example, at page 5 (lines 1-9), page 36 (lines 16-21), page 37, line 25 through page 39, line 21; page 66, line 18 through page 67, line 25; Figure 13, and original claim 31.

Moreover, Applicants respectfully note that, while claim 31 has been through multiple rounds of examination and was previously indicated allowable, this is the first time the Examiner has asserted that the specification lacks support for the claimed molecular conjugate. Pursuant to M.P.E.P. § 707.07(g), "piecemeal examination should be avoided..." and all rejections/objections "on all valid grounds available" should be raised in a timely manner.

Rejection of Claims 57-59 under 35 U.S.C. § 112, First Paragraph – New Matter

Claims 57-59 are rejected as containing new matter. Specifically, the Examiner asserts that the specification and claims do not provide support for a molecular conjugate defined only by SEQ ID NO:2 or SEQ ID NO:4 or a molecular conjugate comprising any monoclonal antibody comprising SEQ ID NOs: 2 and 4.

Applicants respectfully traverse this rejection. Specifically, explicit support for a molecular conjugate defined by the particular heavy and/or light chain variable region sequences of SEQ ID NOs:2 and 4 can be found, at least, for example, in Figure 13. Moreover, to expedite prosecution, Applicants have canceled claim 59 and amended claims 57-58 to specify a *human* monoclonal antibody that includes *both heavy and light chain variable regions*, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 57 and 58 under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 57 and 58 are rejected under 35 U.S.C. § 112, First Paragraph, as not being enabled. Specifically, the Examiner is of the opinion that the specification does not reasonably provide enablement for antibodies defined only by a V_L or V_H region. In support of this argument, the Examiner refers to De Pascalis *et al.* (*J Immunol.* 2002 Sep 15;169(6):3076-84) and Lamminmaki *et al.* (*J Biol Chem.* 2001 Sep 28;276(39):36687-94), which the Examiner characterizes as teaching "that residues from all 6 CDRs participate in antigen binding" and that "while CDR_{H3} plays a prominent role in binding, all CDRs in the V_L also make contact with the antigen."

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 57 and 58 have been amended to specify that the monoclonal antibody includes both

heavy and light chain variable regions. Moreover, while Applicants do not dispute the Examiner's assertion that all 6 CDRs participate in antigen binding and that all CDRs in both the V_L and V_H region make contact with the antigen, this does not mean that claims defining only the heavy or light chain variable region sequence are not enabled. Indeed, once provided with the V_H sequence of a given antibody against a given target antigen, it was well within the ordinary skill of the art to have generated multiple antibodies having the provided V_H sequence paired with different V_L sequences, all of which antibodies retain the ability to bind to the target antigen.

Indeed, prior to the filing of the present application, methods of producing antibodies that bind a specific antigen having a fixed V_L or V_H region and screening a library of complementary variable domains were well known in the art. For example, as evidenced by the enclosed publication by Portolano *et al.* (*The Journal of Immunology* (1993) 150:880-887; enclosed herewith as Appendix A), TPO-binding clones were generated using a single heavy or light chain (known to confer high affinity binding for TPO) to search for other light or heavy chains that could form a Fab capable of binding TPO. Similarly, Clackson *et al.* (Nature (1991) 352:624-628; enclosed herewith as Appendix B) teach the generation of antibodies based on a given V_L or V_H gene sequence by using phage display libraries and selecting for antibodies with particular binding affinities.

In view of these and several other pre-filing publications, it is clear that it was well within the ordinary skill in the art to have generated antibodies against a particular antigen, once provided with a particular V_L or V_H sequence. Further, such references clearly show that the identification and generation of such antibodies would not have required undue experimentation and, in fact, involved routine techniques, such as those described in the Portolano *et al.* and Clackson *et al.* Thus, as evidenced by the prior art teachings and Applicants' specification, the amount of experimentation required to practice the full scope of the presently claimed invention would not have been undue. Importantly, it us well-established that even extensive experimentation is permissible if it is merely routine (see *Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1360 (Fed. Cir. 1998)).

Moreover, as acknowledged by Larry R. Helms (Supervisory Patent Examiner for Art Unit 1643, Technology Center 1600) in his presentation entitled "Enablement Issues in the Examination of Antibodies" in June of 2007 (a copy of which is enclosed herewith as

Appendix C), claims directed to an antibody that binds a specific antigen and comprises a defined V_H or V_L sequence meet the requirements under 35 U.S.C. § 112, first paragraph, for enablement. As recognized by Examiner Helms, disclosure of the V_H or V_L sequences of a given antibody that binds a specific antigen (*e.g.*, the human macrophage mannose receptor) in a patent specification provides sufficient information to have enabled the generation of antibodies having either the provided V_H or V_L sequence paired with complementary chains.

Accordingly, the prior knowledge and skill in the art, combined with the teachings contained in the present specification, would have enabled one skilled in the art to make and use the currently claimed anti-human macrophage mannose receptor antibodies defined by a particular V_L or V_H region, without undue experimentation.

Provisional Obviousness-Type Double Patenting

Claims 31, 38-39, 51-52 and 57-59 are rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 20 and 21 of U.S. Patent Application No.: 10/903,191.

From the outset, claim 59 has been canceled and, therefore, this rejection is moot as applied to this claim. Applicants respectfully traverse this rejection as applied to remaining claims 31, 38-39, 51-52 and 57-58. However, to expedite prosecution, when the pending claims in the present application are indicated as allowable, Applicants will submit, if appropriate, a terminal disclaimer over U.S. Patent Application No.: 10/903,191.

CONCLUSION

In view of the foregoing amendments and arguments, reconsideration and withdrawal of all the rejections and allowance of this application with all pending claims are respectfully requested. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call (617) 227-7400.

Applicants believe no additional fee is due with this response. However, if an additional fee is due, please charge our Deposit Account No. 12-0080, under Order No. CDJ-166CPRCE2 from which the undersigned is authorized to draw.

Dated: March 17, 2008

Respectfully submitted,

By _____

Jill Gormy Sloper
Registration No.: 60,760
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicants